Acute Respiratory and Cardiovascular Outcomes Associated with Low Levels of Ambient Fine Particulate Matter ($PM_{2.5}$) on the Island of Oahu

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Abstract

Scant literature exists regarding health effects of fine particulate matter ($PM_{2.5}$) pollution at or below national standards. This study examined the relationship between $PM_{2.5}$ and acute care use and costs in Honolulu where $PM_{2.5}$ is low. Single and distributed lag over-dispersed Poisson models were used to examine hospitalizations/emergency department (ED) visits associated with cumulative $PM_{2.5}$ exposure over the current day and seven previous days (lags 0-7) in 2011. A 10-$\mu g/m^3$ increase in cumulative $PM_{2.5}$ concentration was associated with a 32% increase in respiratory admissions (RR=1.32, p=0.001) costing $486,908 and a 24% decrease in respiratory admissions in the comparison group (RR=0.76, p<0.001). ED visits increased by 12% at lag day 0 for respiratory outcomes (RR=1.12, p=0.03) and cumulatively with increased respiratory visits by 49% (RR=1.49) and increased combined respiratory and cardiovascular issues by 20% (RR=1.20; p<0.01 for both) costing $117,856. Additional research is needed on health effects within pollution lower levels.

1. Introduction

Particulate matter is generated from fires, road dust, electrical power plants, industrial processes, and vehicles and contributes to air pollution as an ongoing environmental threat to health [1]. Most concerning are very small particles, less than 2.5 micrometers (μ) in width, known as fine particulate matter ($PM_{2.5}$), because they are small enough that they may be inhaled into the cardiopulmonary system. Once inhaled, they may irritate and cause inflammation in the lungs leading to asthma attacks, bronchitis, and decreased lung function [2], as well as the blood vessels around the heart, increasing the risk of heart attack, stroke, arrhythmias, and heart failure, particularly in elderly patients or those with pre-existing medical conditions [3]. These effects were noted in landmark studies such as the Harvard Six Cities study and the American Cancer Society study that demonstrated that higher levels of $PM_{2.5}$ are a causative factor for increased cardiopulmonary disease and mortality risk [4-5].

Further research has demonstrated that exposure to $PM_{2.5}$ is a well-established concern at annual averages above the set current standard (above 12 μ/m^3) with increases of 10 μ/m^3 associated with increased emergency department (ED) visits, hospital admissions, and deaths due to respiratory and cardiovascular adverse health effects [6-10]. Further, increased hospitalizations for mental health [11] as well as increased hospitalizations and mortality due to stroke have also been linked to elevated levels of $PM_{2.5}$ [12]. Several studies have also investigated lag times in relation to health outcomes due to exposure to $PM_{2.5}$ above current acceptable standards with lag periods varying from 2-7 days [7-10]. However, with the exception of a study that showed an inverse association of chronic obstructive pulmonary disease (COPD) exacerbations with a 7-day lag [13] and a study that showed association with arrhythmias, atrial fibrillation, and pulmonary embolism with lags up to four days [14], no other studies have examined the association between current acceptable $PM_{2.5}$ levels with a lag period relative to health outcomes. In terms of health outcomes, the majority of studies have utilized daily counts of hospital admissions or ED visits as measured by International Classification of Diseases 9th revision (ICD-9) or 10th revision (ICD-10) codes. Other methods to determine health outcomes in previous studies included annual patient interviews, Medicare claims counts, disease management groups within a

URI: https://hdl.handle.net/10125/59812
ISBN: 978-0-9981331-2-6

medical practice, and mortality counts. A few have utilized population-based or national inpatient registries.

Based on evidence of harm from exposure to higher levels of $PM_{2.5}$, the World Health Organization (WHO) set criteria for acceptable levels of ambient air pollution and defined that $PM_{2.5}$ should remain below an average of 10 μ/m^3 annually and below 25 μ/m^3 over a 24-hour period [15]. In 2012, the United States (US) Environmental Protection Agency (EPA) also strengthened the health-based standard for $PM_{2.5}$ to an annual level of less than 12 μ/m^3 (previously 15 μ/m^3) and kept the current 24-hour mean at less than 35 μ/m^3 [16]. The EPA reported there was a 42% decrease in the national average $PM_{2.5}$ from 2000 to 2016, with levels well within the more stringent standard in recent years [17].

Only a few studies have examined the impact of $PM_{2.5}$ exposure at levels lower than the current US EPA standards (below 12 μ/m^3), but these also indicate adverse health effects, including increases in hospital admissions for all causes, cardiovascular and respiratory diseases, and mortality [18-20]. These studies were limited to a subset of the total population (e.g., Medicare beneficiaries) and studied aggregated impact rather than examining the effects of daily variation in air quality. Advancing knowledge of the effects of pollution at levels that meet current standards is essential to informing discussions about the impact of making additional changes to air quality standards and related polices such as vehicle emissions. Therefore, the objective of our study is to examine the relationship between daily $PM_{2.5}$ and acute care admissions, with cumulative lag effects up to seven days, across the population in an urban area (Honolulu) that has relatively low levels of this pollutant. We also aimed to explore the costs of these effects.

The average annual exposure of the general public to $PM_{2.5}$ in Hawaii has remained below 12 μ/m^3 as well as below annual averages in the US [21], and the sources of air pollution vary by region within the state. In addition to vehicle and industrial emissions from the urban island of Oahu, volcanic smog ("vog") from the active Kilauea volcano is a key source of $PM_{2.5}$ on the Big Island based on wind patterns, and prior to 2017, sugar cane burning during the pre-harvest season added pollution on the island of Maui. Hawaii Health Information Corporation (HHIC) maintains a robust data set encompassing state-wide, population-wide acute care health information. Previous studies using this data set indicate it holds promise for other air quality research. One study examined the association between sugar cane burning and acute respiratory illness in 2011 in a subset of patients on Maui [22] and another examined the association of pollution from volcanic emissions on ED visits for pulmonary and cardiovascular conditions and used ED visits for fractures as a comparison group expected to be unrelated to pollution [23]. Thus, Hawaii is an ideal location to study associations between relatively low levels of $PM_{2.5}$ and health outcomes.

2. Methods

Honolulu County, comprising the island of Oahu, was the selected region of Hawaii as it has more typical pollution sources and the largest population relative to other areas in the state. The three hospitals outside of the Honolulu area where air quality sensors are located were excluded from the analyses. Data from patients with a home address outside of Hawaii were also excluded to minimize impact of variations in tourist volume on acute care episode frequency.

2.1. Exposure

$PM_{2.5}$ data for 2011 were obtained from the US EPA's Air Quality System database based on the four monitors located in Honolulu County that collected local daily $PM_{2.5}$ conditions (located at downtown Honolulu, Kapolei, Sand Island, and Pearl City). The Hawaii Department of Health (DOH) continuously monitors air quality at each of these sites. The hourly averages are recorded, reviewed, validated, and if needed, revised due to equipment or other technical problems [24-26]. The DOH reports these validated hourly measures to the EPA, and the EPA calculates the daily mean $PM_{2.5}$ concentrations from the hourly data. Daily $PM_{2.5}$ concentrations from all four monitors were averaged for the current study.

2.2. Main Outcome Measures

HHIC collects, cleans, and verifies detailed patient-level discharge data from all non-federal hospitals for all payers across the state of Hawaii. The HHIC dataset contains clinically relevant information used for billing and other administrative purposes. It is not an electronic medical record. The 2011 HHIC dataset of all ED visits (N=110,283) and all hospital admissions (N=74,600) was used to obtain population counts of daily acute care use by reason for admission. These counts include repeat use by the same patient (i.e., these counts are the number of episodes of acute care, not number of unique patients). Reason for each admission was based on All Patient Refined Diagnosis Related Groups (APR DRG) codes, a classification system that describes each admission based on a clinical grouping that can be further described by

severity of illness [27]. We obtained the daily counts of acute care episodes for respiratory and cardiovascular clinical groups, which have previously been found to be associated with high levels of $PM_{2.5}$, and for a comparison group of clinical conditions not expected to be associated with this pollutant (Appendix 1). Because these methods cover all acute care episodes for the population of Honolulu, there was no need to control for age, gender, or other demographic variables.

2.3. Data Analysis

Descriptive statistics were used to characterize daily 2011 $PM_{2.5}$ concentration level and hospital/ED admission outcomes in Honolulu County. Single lag and distributed lag over-dispersed Poisson regression models were used to examine the relative rate (RR) of hospitalizations/ED visits (respiratory, cardiovascular, combined respiratory and cardiovascular, and a comparison group of admissions not expected to be related to increases in acute care use) associated with cumulative exposure over the current day and the seven previous days (lags 0-7). While single lag models assume that the effect in $PM_{2.5}$ is over a single day determined by the lag ℓ, distributed lag models assume that the effect on a given day is spread out over *K* previous days and typically have the form:

$$\log \mu_t = \alpha + \sum_{\ell=0}^{K} \beta_\ell x_{t-\ell} + DOW + s(time, df)$$

where α is the intercept; *K* is the maximum days of lag; β represents the regression coefficient for $PM_{2.5}$; x_t represents $PM_{2.5}$ concentration levels at day *t; DOW* is a dummy variable for day of the week; and *s* is the smoothing spline function for nonlinear variables. In these analyses, models were adjusted for day of the week and smooth functions of calendar time (natural cubic splines) with one degree of freedom. The degrees of freedom (*df*) were selected according to the minimum value of the Akaike information criterion (AIC) for the Poisson model [28], with smaller AIC values indicating the preferred model. According to Peng and Dominici, choosing a large *df* will remove bias but will also remove most of the temporal variation in the residuals and thus lead to a large variance of the estimated air pollution coefficient [29]. Further, choosing a small *df* may lead to bias but also provides a more precise estimate of the air pollution coefficient [29]. Analyses were conducted using hospital and ED admissions, separately. Statistical significance was taken at the 0.05 level. Mean hospitalization and ED costs were estimated using the Centers for Medicare and Medicaid Services (CMS) cost-to-charge ratio (CCR) for fiscal year 2011, which was 0.379 for urban Hawaii [30]. Descriptive statistics were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC) and all other analyses were conducted using the 'dlnm' package in R version 3.4.0.

3. Results

Table 1 displays descriptive statistics for 2011 daily $PM_{2.5}$ and daily hospitalizations/ED visits in Honolulu County. The average daily $PM_{2.5}$ concentration in Honolulu County was 5.71 $\mu g/m^3$ (interquartile range [IQR], 3.85-7.15 $\mu g/m^3$) or average of 45.68 $\mu g/m^3$ cumulative over the 8-day period of interest (0-7 days). For hospitalizations, the daily mean respiratory and cardiovascular admissions were 15.44 (123.52 eight-day cumulative mean) ± 4.60 and 14.80 (118.4 eight-day cumulative mean) ± 3.93, respectively. For ED visits, the daily mean respiratory and cardiovascular admissions were each approximately 25, or 200 for the eight-day cumulative mean (Table 1).

Table 1. Descriptive statistics for 2011 daily $PM_{2.5}$ and daily admissions in Honolulu County

Variable	*Mean ± SD*	*Med (Q25, Q75)*	*Min-Max*
$PM_{2.5}$ (μ/m^3)	5.71 ± 2.70	5.36 (3.85, 7.15)	0.40-26.43
Hospitalizations			
Respiratory admissions	15.44 ± 4.60	15 (12, 18)	6-36
CV admissions	14.80 ± 3.93	15 (12, 18)	5-25
Combined respiratory and CV admissions	30.24 ± 6.41	30 (25, 34)	13-50
Admissions not expected to be related to increases in acute care use	155.69 ± 34.96	166 (122, 185)	80-220
All admissions	204.38 ± 40.83	214 (163, 238)	114-275
ED Visits			
Respiratory admissions	25.21 ± 5.31	25 (21, 28)	14-43
CV admissions	24.35 ± 4.09	24 (22, 27)	13-35
Combined respiratory and CV admissions	49.56 ± 6.96	49 (45, 54)	34-75

Admissions not expected to be related to increases in acute care use	195.34 ± 14.31	195 (185, 205)	153-236
All admissions	302.15 ± 19.96	302 (289, 315)	251-368

CV=Cardiovascular; SD=Standard deviation; Med=Median; Q25=25th percentile; Q75=75th percentile; Min=Minimum; Max=Maximum;

The RR and 95% confidence intervals (CIs) for the increase/decrease in daily admission rates per 10-µg/m^3 increase in $PM_{2.5}$ concentration for single lags of 0, 1, 2, 3, 4, 5, 6, and 7 days (data not shown) and the distributed lag models for lags 0 through 7 for all outcomes were generated. The single lag model estimates the effect of exposure on one day only, lagged by 0, 1, 2, 3, 4, 5, 6, or 7 days, while the cumulative estimate from the distributed lag model represents the effect of eight days of exposure (lag 0 through 7 days) [7]. The cumulative effects of $PM_{2.5}$ on daily admissions over 7 days of lag for all outcomes are displayed in Table 2.

Table 2. Cumulative effects of a 10-µ/m^3 increase in $PM_{2.5}$ on daily admissions in Honolulu County over seven days of lag using distributed lag over-dispersed Poisson regression modeling

Variable	*RR (95% CI)*
Hospitalizations	
Respiratory admissions	1.32 (1.11-1.56)*
CV admissions	0.92 (0.78-1.09)
Combined respiratory and CV admissions	1.11 (0.99-1.24)
Admissions not expected to be related to increases in acute care use	0.76 (0.70-0.82)*
ED Visits	
Respiratory admissions	1.49 (1.32-1.67)*
CV admissions	0.95 (0.86-1.06)
Combined respiratory and CV admissions	1.20 (1.10-1.30)*
Admissions not expected to be related to increases in acute care use	0.96 (0.93-1.01)

CV=Cardiovascular; RR= Relative rate; 95% CI: 95% Confidence interval; *p<0.01

3.1. Hospitalizations

There were no statistically significant single lag estimates for all outcomes, with the exception of the comparison group of admissions not expected to be related to increases in acute care use (data not shown). Specifically, we found evidence of negative associations between day-to-day variation in $PM_{2.5}$ concentration and the control outcome at lag 2 (data not shown; RR=0.96, 95% CI=0.92-1.00, p=0.04), lag 3 (data not shown; RR=0.95, 95% CI=0.91-0.99, p=0.01), and lag 4 (data not shown; RR=0.96, 95% CI=0.92-0.99, p=0.02). Distributed lag model results demonstrated statistically significant 8-day cumulative effects for respiratory admissions and the comparison group admissions. Specifically, there was a 32% increase in respiratory hospital admissions in Honolulu County associated with a 10-µg/m^3 increase in $PM_{2.5}$ over seven days of lag (Table 2; RR=1.32, 95% CI=1.11-1.56, p=0.001). There was a 24% decrease in admissions not expected to be related to increases in acute care use associated with a 10-µg/m^3 increase in $PM_{2.5}$ over seven days of lag (Table 2; RR=0.76, 95% CI=0.70-0.82, p<0.001).

3.2. ED Visits

With the exception of the control outcome, there was at least one exposure lag demonstrating statistical significance for all outcomes. The largest effect was found at lag 0 (same-day) for respiratory ED visits (data not shown; RR=1.12, 95% CI=1.01-1.23, p=0.03). Distributed lag estimates indicated statistically significant 8-day cumulative effects for respiratory visits as well as combined respiratory and cardiovascular visits. Specifically, there was a 49% increase in respiratory ED visits in Honolulu county associated with a 10-µg/m^3 increase in $PM_{2.5}$ over seven days of lag (Table 2; RR=1.49, 95% CI=1.32-1.67, p<0.001). There was a 20% increase in combined respiratory and cardiovascular ED visits associated with a 10-µg/m^3 increase in $PM_{2.5}$ over seven days of lag (Table 2; RR=1.20, 95% CI=1.10-1.30, p<0.001).

3.3. Cost estimates

Table 3 shows the mean cost estimate for each category of hospitalization and ED visit. Using these estimates, each 10-µg/m^3 increase in $PM_{2.5}$ over the 8-day cumulative period of interest is associated with an increase of 39.5 respiratory hospitalizations at a cost of $486,908 and a decrease of 299 hospitalizations unexpected to be related to air pollution at a cost of $3,772,418. Each 10-µg/$m^3$ increase in $PM_{2.5}$ over the 8-day cumulative period of interest is associated with an increase of 79.3 ED visits for respiratory or cardiovascular conditions at a cost of $117,856.

Table 3. Descriptive statistics of cost (in US $) estimated using the CMS cost-to charge ratio (CCR) method for hospitalizations and ED visits in Honolulu County

Variable	*Mean ±SD*	*Med (Q25, Q75)*	*Min-Max*
Hospitalizations			
Respiratory admissions	12,319 ±15,814	7680 (4188, 14199)	0-249, 805
CV admissions	9,107 ±11,642	6463 (3895, 10901)	0-478, 451
Combined respiratory and CV admissions	10,747 ±14,020	7009 (4031, 12539)	0-478, 451
Admissions not related to increases in acute care use	12,620 ±25,911	6831 (2878, 13786)	0-1,169, 869
ED Visits			
Respiratory Admissions	1,416 ±1,287	1003 (561, 1797)	0-12,856
CV admissions	1,560 ±1,356	1222 (737, 1850)	0-37, 179
Combined respiratory and CV admissions	1,486 ±1,323	1131 (633, 1821)	0-37, 179
Admissions not expected to be related to increases in acute care use	1,332 ±1,475	832 (450, 1673)	0-23, 114

CV=Cardiovascular; SD=Standard deviation; Med=Median; Q25=25th percentile; Q75=75th percentile; Min=Minimum; Max= Maximum

4. Discussion

At levels that meet the current more stringent EPA standard, cumulative $PM_{2.5}$ levels over an 8-day period were significantly positively associated with an increase in ED visits and hospital admissions for respiratory conditions, but not cardiovascular conditions. As expected, acute care use for the comparison group of conditions did not increase with air pollution. However, contrary to expectations, hospital admissions for this comparison group decreased significantly with cumulative increases in $PM_{2.5}$. It is possible that the lack of association with acute care use for cardiovascular conditions and the decrease in hospitalizations for comparison group conditions is related to our methodology that counted episodes of care and not individual patients, such that each patient could be counted more than once with multiple episodes of acute care. In addition, each acute care episode is described only by the primary reason for the episode, regardless of other co-existing diagnoses. For example, a high percent of patients with chronic respiratory disease also have overt cardiovascular disease relative to those without respiratory disease [31]. In our study, if the reason for a patient's acute care use is documented as respiratory, it was counted only as a respiratory episode even if the patient had co-morbid cardiovascular disease that exacerbated the respiratory condition in response to increases in pollution.

Research in Australia has found that cardiovascular disease is only one of many co-morbid conditions more common in those with COPD than without [32]. They found that more than 90% of those with COPD, which is one of the most common chronic respiratory diseases, have at least one chronic comorbid condition. These include conditions not previously found to be associated with air quality. For example, within age groups (age 45 to 64; age 65 and older), those with COPD were significantly more likely to report having arthritis and/or back problems compared to those without COPD. To the extent that the most complex and sensitive patients with multiple chronic conditions are hospitalized for respiratory problems, they decrease the count of patients who can present in the emergency department or hospital for other conditions. Thus, additional research is needed using identifiers to determine these relationships at the patient level.

Our research underscores the need for further research on the effects of lower levels of $PM_{2.5}$ and other pollutants on health outcomes to inform policy decisions. Fann and colleagues estimated the number of $PM_{2.5}$-attributable deaths avoided in the US due to decreases in this pollutant from 1980 to 2010 following regulatory action to improve outdoor air quality [33]. Based on previous research, they used two risk coefficients (one log-linear and one non-linear) with regard to the relationship between $PM_{2.5}$ concentration and health outcomes. They estimated that $PM_{2.5}$ decreased by half and that deaths attributable to $PM_{2.5}$ decreased by a third from 1980 to 2010. However, the coefficient assumptions regarding the relationship between lower levels of $PM_{2.5}$ and health outcomes need to be tested to improve the accuracy of these estimates and inform discussions regarding the impact of potential policy changes.

Our research also demonstrates the importance of measuring cumulative effects when studying lower levels of pollution. For example, we found no same-day or lagged-day effects of increases in $PM_{2.5}$ on hospital admissions for respiratory conditions. However, we found a significant increase in respiratory admissions with 8-day cumulative increases in $PM_{2.5}$. While our research used up to a 7-day lag, future research should examine longer lag periods to further explore the impact of variation in air quality at current lower pollution levels. Additional research with data covering multiple years is also needed to increase statistical power. Finally, additional research is needed that controls for variation in temperature and humidity. Absent these controls, Hawaii is an ideal location for such research given that there is little variation in temperature or humidity year-round [34].

Our research demonstrates the value of information systems that track health outcomes population-wide. The all-payer, all-hospital system based on routine administrative data maintained by HHIC has a long history of use in tracking population health indicators. Our current research shows its potential for examining the relationship between these health indicators and environmental variables.

5. Conclusion

Even at relatively low levels of pollution, there is a significant association between increases in $PM_{2.5}$ and frequency of respiratory-related emergency department visits and hospital admissions. Additional research is needed on the impact of pollution at levels currently well within national standards for air quality.

6. Appendices

Appendix 1. All Patient Refined Diagnosis Related Group (APR DRG) codes queried

Type of admissions	*APR DRG codes*
Respiratory admissions	130-131,133-134, 137-144
Cardiovascular admissions	190, 193-194, 196-199, 201, 203-204, 207
Admissions not expected to be related to increases in acute care use (comparison group)	Cardiology (200, 205-206); Cardiovascular surgery (167, 169, 170-171, 173-177, 180); Dental (114); Dermatology (380-381, 384-385); Endocrinology (420-425); ENT surgery (089-93, 095, 097-098); Gastroenterology (241-249, 251-254, 279-280, 282-284); General medicine (812-813, 816, 841-844, 862, 930); General surgery (004-005, 120-121, 135, 220-229, 260-264, 361-364, 401, 403-405, 484, 650-651, 680-681, 710-711, 721-722, 740, 791, 850, 911-912, 950-952); Gynecological surgery (510-514, 517-519, 545) Gynecology (531-532); Hematology (660-661, 663); Infectious disease (049-051, 344, 383, 720, 724, 890, 892-894); Neonatology (580, 583, 588-589, 591, 593, 603, 608-609, 611, 613-614, 621, 623, 625-626, 630-631, 633, 636, 639-640) Nephrology (460, 462-463, 466, 468); Neurological surgery (020-024, 026, 910); Neurology (040, 042-043, 048, 052-053, 055-057); Obstetrics/delivery (540-542, 560); Oncology (041, 240, 281, 343, 382, 461, 500,

	530, 690-694); Open heart surgery (160-163); Ophthalmologic surgery (070, 073); Ophthalmology (080, 082); Orthopedics (340-342, 346-347, 349; Orthopedic surgery (301-305, 308-310, 312-317, 320-321); Other obstetrics (544, 546, 561, 563-566); Otolaryngology (111); Psychiatry (759, 770, 773-776); Rehabilitation (860); Rheumatology (351); Transplant surgery (001, 003); Urological surgery (440-447, 480-483); Urology (465, 501)

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